

## **IN THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Withdrawn) A method for facilitating the termination of cell signalling by a cytokine or cytokine-like molecule, said method comprising promoting interaction between a SOCS-box containing peptide, polypeptide or protein or a chemical analogue thereof and one or more other molecules wherein the resulting complex is subjected to degradation *via* the ubiquitination or proteasomal compartments.
2. (Withdrawn) Use of a SOCS-box-containing peptide, polypeptide or protein or a chemical analogue thereof together with one or more other molecules to couple said SOCS-box-containing peptide, polypeptide or protein and/or one or more other molecules to the ubiquitination or proteasomal compartments thereby terminating or substantially reducing cytokine-or cytokine-like molecule-mediated cell signalling.
3. (Withdrawn) A method according to Claim 1 or 2 wherein the one or more other molecules are elongin B and/or elongin C.
4. (Withdrawn) A method according to Claim 1 or 2 wherein the one or more other molecules are selected from elongin B, elongin C, elongin A or VHL or combinations of elongin B, C and/or A, and/or VHL.
5. (Withdrawn) A method according to claim 1 wherein said peptide, polypeptide or protein or a chemical analogue thereof is encoded by a sequence of nucleotides encoding the amino acid sequence:-

X<sub>1</sub> X<sub>2</sub> X<sub>3</sub> X<sub>4</sub> X<sub>5</sub> X<sub>6</sub> X<sub>7</sub> X<sub>8</sub> X<sub>9</sub> X<sub>10</sub> X<sub>11</sub> X<sub>12</sub> X<sub>13</sub> X<sub>14</sub> X<sub>15</sub> X<sub>16</sub> [X<sub>i</sub>]<sub>n</sub> X<sub>17</sub> X<sub>18</sub> X<sub>19</sub> X<sub>20</sub>  
X<sub>21</sub> X<sub>22</sub> X<sub>23</sub> [X<sub>j</sub>]<sub>n</sub> X<sub>24</sub> X<sub>25</sub> X<sub>26</sub> X<sub>27</sub> X<sub>28</sub>

wherein: X, is L, I, V, M, A or P;

X<sub>2</sub> is any amino acid residue;

X<sub>3</sub> is P, T or S;

X<sub>4</sub> is L, I, V, M, A or P;

$X_5$  is any amino acid;  
 $X_6$  is any amino acid;  
 $X_7$  is L, I, V, M, A, F, Y or W;  
 $X_8$  is C, T or S;  
 $X_9$  is R, K or H;  
 $X_{10}$  is any amino acid;  
 $X_{11}$  is any amino acid;  
 $X_{12}$  is L, I, V, M, A or P;  
 $X_{13}$  is any amino acid;  
 $X_{14}$  is any amino acid;  
 $X_{15}$  is any amino acid;  
 $X_{16}$  is L, I, V, M, A, P, G, C, T or S;  
 $[X_i]_n$  is a sequence of  $n$  amino acids wherein  $n$  is from 1 to 50 amino acids and wherein the sequence  $X_i$  may comprise the same or different amino acids selected from any amino acid residue;  
 $X_{17}$  is L, I, V, M, A or P;  
 $X_{18}$  is any amino acid;  
 $X_{19}$  is any amino acid;  
 $X_{20}$  L, I, V, M, A or P;  
 $X_{21}$  is P;  
 $X_{22}$  is L, I, V, M, A, P or G;  
 $X_{23}$  is P or N;  
 $[X_j]_n$  is a sequence of  $n$  amino acids wherein  $n$  is from 1 to 50 amino acids and wherein the sequence  $X_j$  may comprise the same or different amino acids selected from any amino acid residue;  
 $X_{24}$  is L, I, V, M, A or P;  
 $X_{25}$  is any amino acid;  
 $X_{26}$  is any amino acid;  
 $X_{27}$  is Y or F;  
 $X_{28}$  is L, I, V, M, A or P.

6. (Withdrawn) An agonist or antagonist of cytokine-or cytokine-like molecule-mediated cell signalling, said agonist or antagonist facilitating or otherwise promoting or reducing or otherwise preventing complex formation between two or more of:-
- (i) a SOCS-box-containing peptide, polypeptide or protein or functional equivalent thereof or chemical analogue thereof;
  - (ii) elongin B and/or C or functional equivalents thereof or chemical analogues thereof; and/or
  - (iii) elongin A and/or VHL or functional equivalents thereof or chemical analogues thereof.
7. (Withdrawn) An agonist or antagonist according to Claim 6 wherein said agonist or antagonist is an isolated, naturally occurring molecule.
8. (Withdrawn) A method of modulating activity of SOCS in a human, said method comprising administering to said mammal an effective amount of a molecule for a time and under conditions sufficient to increase or decrease elongin B and/or elongin C binding to a SOCS box.
9. (Withdrawn) A method of modulating levels of a SOCS protein in a cell said method comprising contacting a cell containing a SOCS gene with an effective amount of an inhibitor of elongin B-and/or elongin C-interaction with a SOCS box encoded by said SOCS gene for a time and under conditions sufficient to modulate levels of said SOCS protein.
10. (Withdrawn) A method of modulating signal transduction in a cell containing a SOCS gene comprising contacting said cell with an effective amount of an inhibitor of elongin B and/or elongin C interaction with a SOCS box encoded by said SOCS gene for a time sufficient to modulate levels of SOCS protein with the cell.
11. (Withdrawn) Use of one or more of:-
- (i) elongin B or a functional equivalent or chemical analogue thereof;
  - (ii) elongin C or a functional equivalent or chemical analogue thereof;

- (iii) elongin A or a functional equivalent or chemical analogue thereof;
- (iv) VHL or a functional equivalent or chemical analogue thereof;
- (v) a peptide, polypeptide or protein comprising a SOCS box;
- (vi) an agonist or antagonist of one or more of (i)- (v);
- (vii) an agonist or antagonist of a complex formed by two or more of (i) to (v);
- (viii) a chemical analogue or derivative of one or more of (i)- (vii);

in the manufacture of a medicament in the treatment of a condition in a subject.

12. (Withdrawn) A genetically modified animal comprising a mutation in genetic material encoding a SOCS-box-containing protein such that said SOCS-box in said SOCS-box containing protein is not capable of functionally interacting with one or more of elongin A, B or C, VHL or a cytokine or cytokine-like molecule.

13. (Withdrawn) A method of targeting a protein in a cell for degradation via the ubiquitination or proteasomal compartments in said cell, comprising introducing a polypeptide into said cell, wherein said polypeptide comprises a SOCS box and binds to said protein thereby subjecting said protein to degradation via the ubiquitination or proteasomal compartments in said cell.

14. (Withdrawn) The method of claim 13, wherein said SOCS box interacts with said protein and mediates the binding of said protein to said polypeptide.

15. (Withdrawn) The method of claim 13, wherein said polypeptide further comprises a peptide ligand, wherein said peptide ligand interacts with said protein and mediates the binding of said protein to said polypeptide.

16. (Withdrawn) A method of targeting a protein in a cell for degradation via the ubiquitination or proteasomal compartments in said cell, comprising introducing into said cell a nucleic acid molecule which expresses a polypeptide in said cell, wherein said polypeptide comprises a SOCS box and binds to said protein thereby subjecting said protein to degradation via the ubiquitination or proteasomal compartments in said cell.

17. (Withdrawn) The method of claim 16, wherein said nucleic acid molecule comprises a vector.
18. (Withdrawn) The method of claim 16, wherein said SOCS box interacts with said protein and mediates the binding of said protein to said polypeptide.
19. (Withdrawn) The method of claim 16, wherein said polypeptide further comprises a peptide ligand, wherein said peptide ligand interacts with said protein and mediates the binding of said protein to said polypeptide.
20. (Currently amended) A method of identifying ~~an agent~~ a molecule which inhibits protein degradation in cells mediated by elongin C, comprising subjecting candidate molecules to an assay which detects the interaction between a SOCS box and elongin C wherein said SOCS box comprises the sequence, (T,S,P)LXXX(C,S)XXZX(LIV) (SEQ ID NO:4), and selecting the molecule which inhibits said interaction wherein the selected molecule is a molecule which inhibits protein degradation in cells mediated by elongin C.
21. (Withdrawn) An antagonist identified by the method of claim 20.
22. (Withdrawn) An antagonist identified by the method of claim 20, wherein said molecule binds to elongin C thereby interfering with the binding of said SOCS box to said elongin C.
23. (Currently amended) A method of identifying ~~an agent~~ a molecule which promotes protein degradation in cells mediated by elongin C, comprising subjecting candidate molecules to an assay which detects the interaction between a SOCS box and elongin C wherein said SOCS box comprises the sequence, (T,S,P)LXXX(C,S)XXZX(LIV) (SEQ ID NO:4), and selecting the molecule which promotes said interaction wherein the selected molecule is a molecule which promotes protein degradation in cells mediated by elongin C.
24. (Withdrawn) An agonist molecule identified by the method of claim 23.

25. (Withdrawn) An agonist identified by the method of claim 23, wherein said molecule binds to elongin C thereby interfering with the binding of said SOCS box to said elongin C.